

AMENDMENTS TO THE CLAIMS

The following listing of claims replaces all prior versions, and listings, of claims in this application.

Listing of Claims

1. **(Currently amended)** A method of generating a protein with a polymeric moiety attached at a favorable attachment site comprising:

- a) inputting a set of coordinates for a target protein into a computer;
- b) inputting a set of coordinates for a plurality of polymeric moieties;
- c) selecting a criteria for said favorable attachment site based upon at least one desired characteristic,
- d) analyzing said structure using a simulation module comprising the steps of:
 - i) computationally attaching a plurality of conformers of each of said polymeric moieties to a plurality of amino acids in said target protein; and
 - ii) disallowing conformers at each of said amino acids on the basis of a distance cutoff;
- e) generating a matrix of said amino acids and said polymeric moiety that are energetically favorable;
- f) selecting based upon said criteria one of said amino acids for attachment of one of said polymeric moieties; and
- g) physically making and screening for said at least one desired characteristic said protein with said polymeric moiety attached at said favorable attachment site.

2. **(Previously presented)** A method according to claim 1 wherein said set of polymeric moieties are polymeric conformers.

3. **(Previously presented)** A method according to claim 1 wherein said set of polymeric moieties is generated by chain buildup.

4. **(Withdrawn)** A method according to claim 1 wherein said set of polymeric moieties is generated by utilizing a starting polymeric conformer and perturbing said conformer to generate said set.

5. **(Withdrawn)** A method according to claim 4 wherein said perturbation is done using a Monte Carlo search.

6. **(Withdrawn)** A method according to claim 4 wherein said perturbation is done using a molecular dynamics method.

7. (Original) A method according to claim 1, wherein said protein is a therapeutic protein.

Filed: 3/31/2004

8. **(Previously presented)** A method according to claim 1, wherein said polymeric moiety is pharmaceutically acceptable.
9. **(Previously presented)** A method according to claim 1, wherein said polymeric moieties comprises polyethylene glycol (PEG).
10. **(Previously presented)** A method according to claim 1, wherein said polymeric moiety has a range of about 1000 daltons to about 100,000 daltons.
11. **(Previously presented)** A method according to claim 1, wherein said polymeric moiety is branched.
12. **(Withdrawn)** A method according to claim 1, wherein said polymeric moiety is unbranched.
13. **(Previously presented)** A method according to claim 1, wherein said polymeric moiety is labile.
14. **(Previously Presented)** A method according to claim 1, wherein said simulation module includes Monte Carlo, molecular dynamics or combinations thereof.
15. **(Canceled)**